

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Vega *et al.*
Serial No.: 10/022,249
Confirmation No.: 7196
Filed: December 17, 2001
For: *HIGH THROUGHPUT
DIRECTED EVOLUTION BY
RATIONAL MUTAGENESIS*
Art Unit: 1643
Examiner: Unassigned

TECH CENTER 1600/2900

NOV 13 2002

RECEIVED

02 NOV 13 AM 11:40

RECEIVED
TECH CENTER 1600/2900

TRANSMITTAL LETTER

Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

Transmitted herewith are an Information Disclosure Statement, Forms PTO-1449 (8 pages) and cited references for filing in connection with the above-identified application.

(X) The Commissioner is hereby authorized to charge any fees that may be due under 37 C.F.R. §§ 1.16-1.17 in connection with this paper or with this application during its entire pendency to Deposit Account No. 50- 1213. A duplicate of this sheet is enclosed.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By:


Stephanie L. Seidman
Registration No. 33,779

Date: November 12, 2002
Attorney Docket No. 37851-911
Address all correspondence to:
Stephanie L. Seidman, Esq.
HELLER EHRMAN WHITE & McAULIFFE LLP
4350 La Jolla Village Drive, 7th Floor
San Diego, California 92122-1246
Telephone: (858) 450-8400
Facsimile: (858) 587-5360
EMAIL: sseidman@hewm.com

#9/I.D.S.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Vega *et al.*
Serial No.: 10/022,249
Confirmation No.: 7196
Filed: December 17, 2001
For: *HIGH THROUGHPUT DIRECTED
EVOLUTION BY RATIONAL
MUTAGENESIS*
Art Unit: 1643
Examiner: Unassigned

TECH CENTER 1600/2900

NOV 13 2002

RECEIVED

02 NOV 13 AM 11:40

RECEIVED
TECH CENTER 1600/2900

**INFORMATION DISCLOSURE STATEMENT IN
ACCORDANCE WITH 37 C.F.R. §§ 1.97-1.98**

Commissioner for Patents
U.S. Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

Since this Information Disclosure Statement is filed before the receipt of a first Office Action on the merits for the above-captioned application, no filing fee is due. If it is determined that a fee is due, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-1213.

In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all references known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Forms PTO-1449 (8 pages) and copies of the cited documents are provided herewith.

The cited documents, listed on Forms PTO-1449 and supplied herewith, are in the English language with the exception of items Z, AA and AC. Item Z (WO 01/44809) and item AC (FR 2808645), which are in the French language, are provided with an English language translation and Derwent English language abstract (Item AX) describing the subject matter. Item AA (WO 01/86291), which is in the French language, is provided with a Derwent English language abstract (Item AY) describing the subject matter. Certified English language translations of Items Z and AA will be provided at a later date under separate cover. Hence, in accordance with the requirements of 37 C.F.R. § 1.98, as amended effective March 16, 1992, no further explanation of the listed items is necessary.

Applicant also makes known to the Examiner the following related, co-pending U.S. applications and their status:

U.S.S.N. 10/022,249

Vega et al.

Information Disclosure Statement

U.S.S.N.	Filing Date	Docket No.
10/022,390	12/17/01	912
10/168,075	12/13/00	NA
60/360,085	02/25/02	P918
60/409,898	09/09/02	P922
60/410,258	09/09/02	P923

Foreign App. No.	Filing Date
EP 00985423.3	12/13/00
PCT/IB02/03921	08/16/02
Unassigned	08/16/02

Although these documents are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the references, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. §1.97(h), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. §1.56(b) exists.

Applicant respectfully requests that the Examiner review the foregoing references and information and that they be made of record in the file history of the above-captioned application.

* * *

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By:

Stephanie Seidman
Registration No. 33,779

Dated: November 12, 2002

Attorney Docket No.: 37851-911

Address all correspondence to:

Stephanie Seidman, Esq.

HELLER EHRMAN WHITE & McAULIFFE LLP

4350 La Jolla Village Drive, 7th Floor

San Diego, California 92122

Telephone: (858) 450-8400

Facsimile: (858) 587-5360

EMAIL: sseidman@hewm.com

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643

LIST OF PATENTS AND PUBLICATIONS FOR
APPLICANT'S INFORMATION DISCLOSURE
STATEMENT

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER							DATE	NAME	CLASS	SUB CLASS	FILING DATE
	A	4	7	9	7	3	6	8	01/10/89	Carter <i>et al.</i>	435	320	03/15/85
	B	5	1	3	9	9	4	1	08/18/92	Muzyczka <i>et al.</i>	435	172.3	10/25/91
	C	5	5	7	1	6	9	8	11/05/96	Ladner <i>et al.</i>	435	69.7	06/18/93
	D	5	7	2	3	3	2	3	03/03/98	Kauffman <i>et al.</i>	435	172.3	12/02/94
	E	5	7	5	3	5	0	0	05/19/98	Shenk <i>et al.</i>	435	320.1	04/03/95
	F	5	7	6	3	2	3	9	06/09/98	Short <i>et al.</i>	435	172.1	06/18/96
	G	5	7	7	0	4	3	4	06/23/98	Huse	435	252.33	05/15/95
	H	5	7	7	9	4	3	4	07/14/98	De Long	415	104	02/06/97
	I	5	7	9	8	3	9	0	08/25/98	Weber <i>et al.</i>	514	634	05/22/95
	J	5	8	3	7	5	0	0	11/17/98	Ladner <i>et al.</i>	435	69.7	04/03/95
	K	5	8	6	2	5	1	4	01/19/99	Huse <i>et al.</i>	702	22	12/06/96
	L	5	8	7	1	9	7	4	02/16/99	Huse	435	69.7	12/02/94
	M	6	0	0	1	5	7	4	12/14/99	Short <i>et al.</i>	435	6	03/04/98
	N	6	0	5	7	1	0	3	05/02/00	Short	435	6	08/26/97
	O	6	0	9	6	5	4	8	08/01/00	Stemmer	435	440	02/03/97
	P	6	1	1	7	6	7	9	09/12/00	Stemmer	435	440	05/25/96
	Q	6	1	2	7	1	7	5	10/03/00	Vigne <i>et al.</i>	435	325	07/17/97
	R	6	1	3	2	9	7	0	10/17/00	Stemmer	435	6	06/19/98
	S	6	1	5	6	5	0	9	12/05/00	Schellenberger	435	6	11/12/97
	T	6	1	6	5	7	9	3	12/26/00	Stemmer	435	440	05/08/98
	U	6	1	7	1	8	2	0	01/09/01	Short	435	69.1	02/04/99
	V	6	1	7	4	6	7	3	01/16/01	Short <i>et al.</i>	435	6	06/16/98
	W	6	1	8	0	4	0	6	01/30/01	Stemmer	435	440	06/17/98
	X	6	2	3	8	8	8	4	05/29/01	Short <i>et al.</i>	435	69.1	03/09/99

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

RECEIVED
NOV 13 2002
TECH CENTER 1600/2900

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643

LIST OF PATENTS AND PUBLICATIONS FOR
APPLICANT'S INFORMATION DISCLOSURE
STATEMENT

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER							DATE	NAME	CLASS	SUB CLASS	FILING DATE
	Y	6	2	5	8	5	3	0	07/10/01	Huse	435	6	12/30/94

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUB CLASS	Translation Yes No	
	Z	0	1	4	4	8	0	9	06/21/01	PCT			X	
	AA	0	1	8	6	2	9	1	11/15/01	PCT				X*
	AB	9	9	1	1	7	6	4	03/11/99	PCT				
	AC	2	8	0	2	6	4	5	12/16/99	FR				X*

X* = An English Language Derwent Abstract is Provided.

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AD	Ashktorab <i>et al.</i> , "Identification of Nuclear Proteins That Specifically Interact with Adeno-Associated Virus Type 2 Inverted Terminal Repeat Hairpin DNA", <i>Journal of Virology</i> , <u>63</u> :3034-3039 (1989)
AE	ATCC accession no. VR-646, "Adeno-associated virus 4 deposited as Adeno-associated virus type 4", (accessed on 09/05/2002)
AF	ATCC accession no. VR-1449, "Simian virus 15", (accessed on 09/05/2002)
AG	ATCC accession no. VR-680, "Adeno-associated virus 2 deposited as Adeno-associated virus type 2", (accessed on 09/05/2002)
AH	ATCC accession no. VR-681, "Adeno-associated virus 3 deposited as Adeno-associated virus type 3", (accessed on 09/05/2002)
AI	ATCC accession no. VR-645, "Adeno-associated virus 1 deposited as Adeno-associated (satellite) virus type 1", (accessed on 09/05/2002)
AJ	Atkinson <i>et al.</i> , "A high-throughput hybridization method for titer determination of viruses and gene therapy vectors", <i>Nucleic Acids Research</i> , <u>26</u> :2821-2823 (1998)
AK	Altschul <i>et al.</i> , "Basic Local Alignment Search Tool", <i>J. Molec. Biol.</i> , <u>215</u> :403-410 (1990)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT		

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AL	Batchu <i>et al.</i> , "Disassociation of Conventional DNA Binding and Endonuclease Activities by an Adeno-Associated Virus Rep78 Mutant", <i>Biochemical And Biophysical Research Communications</i> , <u>210</u> :717-725 (1995)
AM	Beaton <i>et al.</i> , "Expression from the Adeno-Associated Virus p5 and p19 Promoters Is Negatively Regulated in <i>trans</i> by the <i>rep</i> Protein", <i>Journal of Virology</i> , <u>63</u> :4450-4454 (1989)
AN	Beck-Sickinger <i>et al.</i> , "Complete L-alanine scan of neuropeptide Y reveals ligands binding to Y ₁ and Y ₂ receptors with distinguished conformations", <i>Eur. J. Biochem.</i> , <u>223</u> :947-958 (1994)
AO	Carillo <i>et al.</i> , "The Multiple Sequence Alignment Problem in Biology", <i>SIAM J. Applied Math</i> , <u>48</u> :1073-1082 (1988)
AP	Cassinotti <i>et al.</i> , "Organization of the Adeno-Associated Virus (AAV) Capsid Gene: Mapping of a Minor Spliced mRNA Coding for Virus Capsid Protein 1", <i>Virology</i> , <u>167</u> :176-184 (1988)
AQ	Chadeuf <i>et al.</i> , "Efficient recombinant adeno-associated virus production by a stable rep-cap HeLa cell line correlates with adenovirus-induced amplification of the integrated rep-cap genome", <i>J. Gene Med.</i> , <u>2</u> :260-268 (2000)
AR	Chejanovsky <i>et al.</i> , "Mutation of a Consensus Purine Nucleotide Binding Site in the Adeno-Associated Virus <i>rep</i> Gene Generates a Dominant Negative Phenotype for DNA Replication", <i>J. Virology</i> , <u>64</u> :1764-1770 (1990)
AS	Chejanovsky <i>et al.</i> , "Mutagenesis of an AUG Codon in the Adeno-Associated Virus <i>rep</i> Gene: Effects on Viral DNA Replication", <i>J. Virology</i> , <u>173</u> :120-128 (1989)
AT	Cullen <i>et al.</i> , "Analysis of the Physical State of Different Human Papillomavirus DNAs in Intraepithelial and Invasive Cervical Neoplasm", <i>Journal of Virology</i> , <u>65</u> :606-612 (1991)
AU	Davis <i>et al.</i> , "Mutational Analysis of Adeno-Associated Virus Type 2 Rep68 Protein Endonuclease Activity on Partially Single-Stranded Substrates", <i>Journal of Virology</i> , <u>74</u> :2936-2942 (2000)
AV	Davis <i>et al.</i> , "Analysis of the Effects of Charge Cluster Mutations in Adeno-Associated Virus Rep68 Protein In Vitro", <i>Journal of Virology</i> , <u>73</u> :2084-2093 (1999)
AW	Deng <i>et al.</i> , "Site-Directed Mutagenesis of Virtually Any Plasmid by Eliminating a Unique Site", <i>Analytical Biochemistry</i> , <u>200</u> :81-88 (1992)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

FORM PTO-1449 (Modified) LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AX	Derwent # 013914049, WPI Acc. No. 2001-398262/200142, for French Patent FR 2802645 and PCT Patent Application WO 2001/44809 "Evaluating the performance of complex biological agents in target cells, for selecting gene therapy vectors with optimal properties, comprises constructing a theoretical curve"
AY	Derwent # 014262217, WPI Acc. No. 2002-082915/200211, for PCT Patent Application WO 2001/86291 A1, "Determining titer of biological agent, useful e.g. for gene therapy vectors or vaccines, is based on measuring reaction with cells at constant concentration, over a specified time period"
AZ	Devereux <i>et al.</i> , "A comprehensive set of sequence analysis programs for the VAX", <i>Nucleic Acids Research</i> , <u>12</u> (1):387-395 (1984)
BA	Drittanti <i>et al.</i> , "High throughput production, screening and analysis of adeno-associated viral vectors", <i>Gene Therapy</i> , <u>7</u> :924-929 (2000)
BB	Drittanti <i>et al.</i> , "Optimised helper virus-free production of high-quality adeno-associated virus vectors", <i>The Journal of Gene Medicine</i> , <u>3</u> :59-71 (2001)
BC	Du <i>et al.</i> , "Efficient transduction of human neurons with an adeno-associated virus vector", <i>Gene Therapy</i> , <u>3</u> :254-261 (1996)
BD	Gavin <i>et al.</i> , "Charge-to-Alanine Mutagenesis of the Adeno-Associated Virus Type 2 Rep78/68 Proteins Yields Temperature-Sensitive and Magnesium-Dependent Variants", <i>Journal of Virology</i> , <u>73</u> :9433-9445 (1999)
BE	Genbank accession no. NC_002077, Nucleotide, "Adeno-associated virus 1, complete genome", (accessed on 09/05/2002)
BF	Genbank accession no. NC_001829, Nucleotide, "Adeno-associated virus 4, complete genome", (accessed on 09/05/2002)
BG	Genbank accession no. NC_001863, Nucleotide, "Adeno-associated virus 3B, complete genome", (accessed on 09/05/2002)
BH	Genbank accession no. NC_001401, Nucleotide, "Adeno-associated virus 2, complete genome", (accessed on 09/05/02)
BI	Genbank accession no. NC_001729, Nucleotide, "Adeno-associated virus 3, complete genome", (accessed on 09/05/02)
BJ	Gibbs <i>et al.</i> , "Rational Scanning Mutagenesis of a Protein Kinase Identifies Functional Regions Involved in Catalysis and Substrate Interactions", <i>Journal of Biology Chemistry</i> , <u>266</u> :8923-8931 (1991)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643

LIST OF PATENTS AND PUBLICATIONS FOR
APPLICANT'S INFORMATION DISCLOSURE
STATEMENT

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

BK	Gribskov <i>et al.</i> , "Sigma factors from <i>E. coli</i> , <i>B. subtilis</i> , phage SP01, and phage T4 are homologous proteins", <i>Nucleic Acids Research</i> , <u>14</u> :6745-6763 (1986)
BL	Hermonat, P.L., "Down-regulation of the human <i>c-fos</i> and <i>c-myc</i> proto-oncogene promoters by adeno-associated virus Rep78", <i>Cancer Letters</i> , <u>81</u> :129-136 (1994)
BM	Hermonat <i>et al.</i> , "Genetics of Adeno-Associated Virus: Isolation and Preliminary Characterization of Adeno-Associated Virus Type 2 Mutants", <i>Journal of Virology</i> , <u>51</u> :329-339 (1984)
BN	Hill A.V., "The possible effects of the aggregation of the molecules of haemoglobin on its dissociation curves", <i>Proceedings of the Physiological, Journal of Physiology</i> , <u>40</u> :iv-vii (1910)
BO	Hill <i>et al.</i> , "XLVII. The Combinations Of Haemoglobin With Oxygen And With Carbon Monoxide", <i>I. Biochem. J.</i> , <u>7</u> :471-480 (1913)
BP	Horer <i>et al.</i> , "Mutational Analysis of Adeno-Associated Virus Rep Protein-Mediated Inhibition of Heterologous and Homologous Promoters", <i>Journal of Virology</i> , <u>69</u> :5485-5496 (1995)
BQ	Im <i>et al.</i> , "Partial Purification of Adeno-Associated Virus Rep78, Rep52, and Rep40 and Their Biochemical Characterization", <i>Journal of Virology</i> , <u>66</u> :1119-1128 (1992)
BR	Im <i>et al.</i> , "The AAV Origin Binding Protein Rep68 Is an ATP-Dependent Site-Specific Endonuclease with DNA Helicase Activity", <i>Cell</i> , <u>61</u> :447-457 (1990)
BS	Kechli <i>et al.</i> , "Expression of the Human Immunodeficiency Virus Type 1 Primer Binding Sequence Inhibits HIV-1 Replication", <i>Human Gene Therapy</i> , <u>9</u> :587-590 (1998)
BT	Kyostio <i>et al.</i> , "Negative Regulation of the Adeno-Associated Virus (AAV) P ₅ Promoter Involves both the P ₅ Rep Binding Site and the Consensus ATP-Binding Motif of the AAV Rep68 Protein", <i>Journal of Virology</i> , <u>69</u> :6787-6796 (1995)
BU	Kyostio <i>et al.</i> , "Identification of Mutant Adeno-Associated Virus Rep Proteins Which Are Dominant-Negative For DNA Helicase Activity", <i>Biochemical and Biophysical Research Communications</i> , <u>220</u> :294-299 (1996)
BV	Kyostio <i>et al.</i> , "Analysis of Adeno-Associated Virus (AAV) Wild-Type and Mutant Rep Proteins for Their Abilities To Negatively Regulate AAV p ₅ and p ₁₉ mRNA Levels", <i>Journal of Virology</i> , <u>68</u> :2957-2957 (1994)
BW	Marcello <i>et al.</i> , "Adeno-Associated Virus Type 2 Rep Protein Inhibits Human Papillomavirus Type 16 E2 Recruitment of the Transcriptional Coactivator p300", <i>Journal of Virology</i> , <u>74</u> :9090-9098 (2000)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643
LIST OF PATENTS AND PUBLICATIONS FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT		

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

BX	Matsushita <i>et al.</i> , "Localization of von Willebrand Factor-binding Sites for Platelet Glycoprotein Ib and Botrocetin by Charged-to-Alanine Scanning Mutagenesis", <i>Journal of Biology Chemistry</i> , <u>275</u> :11044-11049 (2000)
BY	McCarty <i>et al.</i> , "Analysis of Mutations in Adeno-Associated Virus Rep Protein In Vivo and In Vitro", <i>Journal of Virology</i> , <u>66</u> :4050-4057 (1992)
BZ	Mendelson <i>et al.</i> , "Identification of the <i>trans</i> -Acting Rep Proteins of Adeno-Associated Virus by Antibodies to a Synthetic Oligopeptide", <i>Journal of Virology</i> , <u>60</u> :823-832 (1986)
CA	Mittereder <i>et al.</i> , "Evaluation of the Concentration and Bioactivity of Adenovirus Vectors for Gene Therapy", <i>Journal of Virology</i> , <u>70</u> :7498-7509 (1996)
CB	Needleman <i>et al.</i> , "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins", <i>Journal of Molec. Biol.</i> , <u>48</u> :443 (1970)
CC	Nelson <i>et al.</i> , "Characterization of Diverse Viral Vector Preparations, Using a Sample and Rapid Whole-Virion Dot-Blot Method", <i>Hum. Gene Ther.</i> , <u>9</u> :2401-2405 (1998)
CD	Ni <i>et al.</i> , "In Vitro Replication of Adeno-Associated Virus DNA", <i>Journal of Virology</i> , <u>68</u> :1128-1138 (1994)
CE	Owens <i>et al.</i> , "Identification of a DNA-Binding Domain in the Amino Terminus of Adeno-Associated Virus Rep Proteins," <i>J. Virology</i> , <u>67</u> (2):997-1005 (1993)
CF	Owens <i>et al.</i> , "In Vitro Resolution of Adeno-Associated Virus DNA Hairpin Termini by Wild-Type Rep Protein Is Inhibited by a Dominant-Negative Mutant of Rep", <i>Journal of Virology</i> , <u>66</u> :1236-1240 (1992)
CG	Owens <i>et al.</i> , "Adeno-Associated Virus Rep Proteins Produced in Insect and Mammalian Expression Systems: Wild-Type and Dominant-Negative Mutant Proteins Bind to the Viral Replication Origin", <i>Journal of Virology</i> , <u>184</u> :14-22 (1991)
CH	Pearson <i>et al.</i> , "Improved tools for biological sequence comparison", <i>Proc. Natl. Acad. Sci. USA</i> , <u>85</u> :2444 (1988)
CI	Press Release 11; "Nautilus Biotech granted patent covering molecular fitness analysis with key applications in directed evolution and functional genomics target identification"; Paris- February 6, 2002; http://www.nautilusbiotech.com/news-pressrelease11.php3 , accessed on (2/28/02)
CJ	Press Release 10; "Nautilus Biotech and Microbix Biosystems, Inc. (TSE: MBX) sign a distribution agreement for rAAV high-producer cells"; Paris- January 11, 2002; http://www.nautilusbiotech.com/news-pressrelease10.php3 , accessed on (2/28/02)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643

LIST OF PATENTS AND PUBLICATIONS FOR
APPLICANT'S INFORMATION DISCLOSURE
STATEMENT

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CK	Press Release 7; "Nautilus Biotech optimizes the AAV rep protein to increase rAAV productivity"; Paris- September 21, 2001; http://www.nautilusbiotech.com/news-pressrelease7.php3 , accessed on (2/28/02)
CL	Press Release 6; "Nautilus Biotech S.A. Files a Key Patent Application in the U.S."; Paris- September 14, 2001; http://www.nautilusbiotech.com/news-pressrelease6.php3 , accessed on (2/28/02)
CM	Ropp <i>et al.</i> , "Aequorea Green Fluorescent Protein Analysis by Flow Cytometry", <i>Cytometry</i> , <u>21</u> :309-317 (1995)
CN	Ruffing <i>et al.</i> , "Mutations in the carboxy terminus of adeno-associated virus 2 capsid proteins affect viral infectivity: lack of an RGD integrin-binding motif", <i>J. Gen. Virol.</i> , <u>75</u> :3385-3392 (1994)
CO	Ryan <i>et al.</i> , "Sequence Requirements for Binding of Rep68 to the Adeno-Associated Virus Terminal Repeats", <i>Journal of Virology</i> , <u>70</u> :1542-1553 (1996)
CP	Salveti <i>et al.</i> , "Factors Influencing Recombinant Adeno-Associated Virus Production", <i>Hum. Gene Ther.</i> , <u>20</u> :695-706 (1998)
CQ	Samulski <i>et al.</i> , "A Recombinant Plasmid from Which an Infectious Adeno-Associated Virus Genome Can Be Excised In Vitro and Its Use To Study Viral Replication", <i>Journal of Virology</i> , <u>61</u> :3096-3101 (1987)
CR	Schwartz <i>et al.</i> , "Matrices for Detecting Distant Relationships", Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, pp. 353-358 (1978)
CS	Smith <i>et al.</i> , "Comparison of Biosequences", <i>Advances in Applied Mathematics</i> , <u>2</u> :482-489 (1981)
CT	Smith <i>et al.</i> , "Single-step purification of polypeptides expressed in <i>Escherichia coli</i> as fusions with glutathione S-transferase", <i>Gene</i> , <u>67</u> :31-40 (1988)
CU	Srivastava <i>et al.</i> , "Nucleotide Sequence and Organization of the Adeno-Associated Virus 2 Genome", <i>Journal of Virology</i> , <u>45</u> :555-564 (1983)
CV	Tessier <i>et al.</i> , "Characterization of Adenovirus-Induced Inverted Terminal Repeat-Independent Amplification of Integrated Adeno-Associated Virus <i>rep-cap</i> Sequences", <i>Journal of Virology</i> , <u>75</u> :375-383 (2001)
CW	Translation of PCT Patent Application WO 01/44809, "Methods for Screening or Assessing the Performance of a Collection of Biological Agents in Living Parget Cells, And Their Applications"

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**

FORM PTO-1449 (Modified)	ATTY. DOCKET NO. 37851-0911	SERIAL NO. 10/022,249
	APPLICANT VEGA et al.	
	FILING DATE December 17, 2001	GROUP 1643

LIST OF PATENTS AND PUBLICATIONS FOR
APPLICANT'S INFORMATION DISCLOSURE
STATEMENT

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

CX	Urabe <i>et al.</i> , "Charged-to-Alanine Scanning Mutagenesis of the N-Terminal Half of Adeno-Associated Virus Type 2 Rep78 Protein", <i>Journal of Virology</i> , <u>23</u> :2682-2693 (1999)
CY	Walker <i>et al.</i> , "Mutational Analysis of the Adeno-Associated Virus Type 2 Rep68 Protein Helicase Motifs", <i>Journal of Virology</i> , <u>71</u> :6996-7004 (1997)
CZ	Walker <i>et al.</i> , "Mutational Analysis of the Adeno-Associated Virus Rep68 Protein: Identification of Critical Residues Necessary for Site-Specific Endonuclease Activity", <i>Journal of Virology</i> , <u>71</u> :2722-2730 (1997)
DA	Watson <i>et al.</i> , " <i>Molecular Biology of the Gene</i> ", 4th Ed., The Benjamin/Cummings Pub. Co., p. 224, (1987)
DB	Weitzman <i>et al.</i> , "Interaction of Wild-Type and Mutant Adeno-Associated Virus (AAV) Rep Proteins on AAV Hairpin DNA", <i>Journal of Virology</i> , <u>70</u> :2240-2248 (1996)
DC	Weitzman <i>et al.</i> , "Recruitment of Wild-Type and Recombinant Adeno-Associated Virus into Adenovirus Replication Centers", <i>Journal of Virology</i> , <u>70</u> :1845-1854 (1996)
DD	Wu <i>et al.</i> , "Mutational Analysis of the Adeno-Associated Virus Type 2 (AAV2) Capsid Gene and Construction of AAV2 Vectors with Altered Tropism", <i>J. Virol.</i> , <u>74</u> :8635-8647 (2000)
DE	Yang <i>et al.</i> , "Mutational Analysis of the Adeno-Associated Virus <i>rep</i> Gene", <i>Journal of Virology</i> , <u>66</u> :6058-6069 (1992)
DF	Yang <i>et al.</i> , "Analysis of the Terminal Repeat Binding Abilities of Mutant Adeno-Associated Virus Replication Proteins", <i>Journal of Virology</i> , <u>67</u> : 4442-4447 (1993)
DG	Yoon <i>et al.</i> , "Amino-Terminal Domain Exchange Redirects Origin-Specific Interactions of Adeno-Associated Virus Rep78 In Vitro", <i>Journal of Virology</i> , <u>75</u> :3230-3239 (2001)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Title: **HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS**